RECEIVED
CENTRAL FAX CENTER
SEP 15 2008

> responsive element (HRE), wherein the adenovirus gene is selected from the group consisting of an E1B gene, an E2A gene, an E2B gene, and an E4 gene, wherein the transgene is a suicide gene selected from the group consisting of a TNF-α gene, a Trail gene, a Bax gene, an HSV-tk gene, a cytosine deaminase gene, a p450 gene, and a diphtheria toxin gene, an s-Flt1 gene, and an ex-Flk1 gene.

Support for the amendment to claim 1 can be found throughout the specification as filed and particularly at page 6, lines 19-27, and in original claim 2. No new matter has been added.

Accordingly, present claim 1 is directed to an adenovirus vector comprising an adenovirus gene and a transgene, each under the transcriptional control of a TRE comprising an HRE, wherein the adenovirus gene is selected from the group consisting of an E1B gene, an E2A gene, an E2B gene, and an E4 gene, and wherein the transgene is a suicide gene. Applicants respectfully submit that Van Meir et al. does not teach an adenovirus vector comprising an adenovirus gene and a transgene, wherein the adenovirus gene is selected from the group consisting of an E1B gene, an E2A gene, an E2B gene, and an E4 gene, and which is under the control of a TRE, as currently recited in claim 1.

The Patent Office refers to page 34, lines 1-2 of Van Meir et al., which recites "Recombinant viruses were able to express constitutively (Ad-CMV-E1) or conditionally (HYPR-Ad1) E1A and E1B gene products.". *See*, page 6 of the Official Action. Accordingly, it appears that the Patent Office is asserting that this disclosure in Van Meir et al. teaches an adenovirus vector comprising two adenovirus genes under the transcriptional control of a TRE, including an E1B gene.

However, applicants respectfully disagree. In particular, the paragraph preceding the excerpt of Van Meir et al. cited by the Patent Office, at page 33, lines 25-29, states the following:

> E1A is activated by hypoxia in HYPR-Ad1. E1A is known to activate the expression of other viral promoters including early E1B gene regulation. This explains the increased expression of E1B gene products under hypoxia. Late E1B gene regulation involves other factors and may explain the increased expression of E1B21K under normoxia at 2-3 days post-infection.

(emphasis added).

As such, in contrast to the apparent assertion by the Patent Office, Van Meir et al. does not teach an adenovirus vector comprising two adenovirus genes, wherein each is under the transcriptional control of a TRE. In marked contrast, Van Meir et al., at best, discloses an adenovirus vector with an E1B gene that is regulated by E1A. As such, applicants respectfully submit that Van Meir et al. fails to disclose an adenovirus vector comprising two adenovirus genes and a transgene, wherein both adenovirus genes and the transgene are each under the transcriptional control of a TRE, as recited in claim 3. Furthermore, applicants respectfully submit that Van Meir et al. does not teach an adenovirus vector comprising an adenovirus gene and transgene, wherein the adenovirus gene selected from E1B, E2A, E2B and E4 is under the transcriptional control of a TRE, as recited in present claim 1. Thus, applicants respectfully submit that Van Meir et al. fails to support a rejection of claim 1 under 35 U.S.C. §102(a/e).